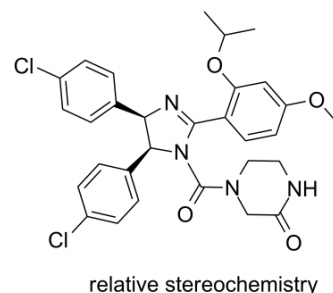


Nutlin-3

Cat. No.:	HY-50696		
CAS No.:	548472-68-0		
Molecular Formula:	C ₃₀ H ₃₀ Cl ₂ N ₄ O ₄		
Molecular Weight:	581.49		
Target:	MDM-2/p53; E1/E2/E3 Enzyme		
Pathway:	Apoptosis; Metabolic Enzyme/Protease		
Storage:	Powder	-20°C	3 years
		4°C	2 years
	In solvent	-80°C	6 months
		-20°C	1 month



SOLVENT & SOLUBILITY

In Vitro

DMSO : ≥ 50 mg/mL (85.99 mM)
 * "≥" means soluble, but saturation unknown.

Preparing Stock Solutions	Solvent Concentration	Mass		
		1 mg	5 mg	10 mg
	1 mM	1.7197 mL	8.5986 mL	17.1972 mL
	5 mM	0.3439 mL	1.7197 mL	3.4394 mL
	10 mM	0.1720 mL	0.8599 mL	1.7197 mL

Please refer to the solubility information to select the appropriate solvent.

In Vivo

- Add each solvent one by one: 10% DMSO >> 40% PEG300 >> 5% Tween-80 >> 45% saline
 Solubility: ≥ 2.5 mg/mL (4.30 mM); Clear solution
- Add each solvent one by one: 10% DMSO >> 90% corn oil
 Solubility: ≥ 2.5 mg/mL (4.30 mM); Clear solution

BIOLOGICAL ACTIVITY

Description

Nutlin-3 is a commercial available p53-MDM2 inhibitor, with K_i of 90 nM.

IC₅₀ & Target

K_i: 90 nM (p53-MDM2)^[1]

In Vitro

Nutlin-3 is an inhibitor of the MDM2-p53 interaction. In particular, co-treatment of p53-positive HCT116 cells with 1 μM of Inauhzin and 2 μM of Nutlin-3 more significantly activated p53 as measured by its protein level as well as the level of its target p21, PUMA or cleaved PARP as indication of apoptosis^[2]. Nutlin-3 is a small-molecule inhibitor that acts to inhibit MDM2 binding to p53 and subsequent p53-dependent DNA damage signaling. As a single agent, Nutlin-3 (2-10 μM) stabilizes p53 and p21^{WAF} levels and is toxic to WTP53-22RV1 cells (IC₅₀, 4.3 μM) but has minimal toxicity toward p53-deficient cells (IC

$50, >10 \mu\text{M}$). Nutlin-3 induces p53 and p21^{WAF} expression in a dose-dependent manner in 22RV1 cells. Short-term cell cycle assays show that, at a dose of 10 μM , Nutlin-3 increases slightly the G₁-phase fraction and decreases the S-phase fraction of all three cell lines^[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

In Vivo

Nutlin-3 can suppress the growth of xenograft tumors derived from human osteosarcoma or leukemia cells, the anti-tumor activity of Nutlin-3 even at the dose of 200 mg/kg per oral administration is marginal in an HCT116-derived xenograft tumor model^[2]. Nutlin-3 may be a useful adjunct to improve the therapeutic ratio using precision radiotherapy targeted to hypoxic cells and warrants further study in vivo^[3].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

PROTOCOL

Cell Assay ^[2]

Human non-small-cell lung carcinoma wild type p53-containing H460 and A549, human non-small-cell lung carcinoma p53-null H1299, and human colon cancer HCT116 (p53^{+/+} and p53^{-/-}) cells are used. Cells (1.5×10^5) are plated into 6-well plates, and incubated at 37°C overnight. After treatment of Inauhzin and Nutlin 3 at the indicated concentrations for 48 h, cells are harvested, fixed in 70% ice-cold ethanol overnight at -20°C, resuspended in propidium iodide-solution (50 $\mu\text{g}/\text{mL}$ PI, 0.1 mg/mL RNase A, 0.05% Tritin X-100 in PBS) for 40 min at 37°C, then analyzed for DNA content using a flow cytometer and proprietary software^[2].

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

Animal Administration ^[2]

Mice^[2]

Five-week-old female SCID mice are used. Mice are subcutaneously inoculated with 3×10^6 HCT116^{p53+/+} cells in the right flank and tumor growth is monitored with calipers. After the mean tumor volume reaches 50-100 mm³, animals are administered Inauhzin intraperitoneally (IP), Nutlin 3 orally, or vehicles (4% DMSO for Inauhzin, EtOH: Tween: 5% Glucose=5:5:90 for Nutlin 3). Tumor volume is measured every other day, and inhibition of tumor growth (T/C) is calculated on the last day of treatment.

MCE has not independently confirmed the accuracy of these methods. They are for reference only.

CUSTOMER VALIDATION

- Cancer Res. 2019 Feb 1;79(3):534-545.
- Cell Death Dis. 2020 Nov 12;11(11):976.
- Mater Sci Eng C Mater Biol Appl. 2020 Mar;108:110403.
- EBioMedicine. 2019 Oct;48:248-263.
- Sci Rep. 2019 Nov 19;9(1):17050.

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REFERENCES

- [1]. Yu Z, et al. Design, synthesis and biological evaluation of sulfamide and triazole benzodiazepines as novel p53-MDM2 inhibitors. *Int J Mol Sci.* 2014 Sep 5;15(9):15741-53.
- [2]. Zhang Y, et al. Inauhzin and Nutlin3 synergistically activate p53 and suppress tumor growth. *Cancer Biol Ther.* 2012 Aug;13(10):915-24.
- [3]. Supiot S, et al. Nutlin-3 radiosensitizes hypoxic prostate cancer cells independent of p53. *Mol Cancer Ther.* 2008 Apr;7(4):993-9.

Caution: Product has not been fully validated for medical applications. For research use only.

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